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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/689,366	10/12/2000	Mike Rothe	T95-005-2	7997

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HILLSBOROUGH, CA 94010

EXAMINER

LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 12/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

OSM

Advisory Action

Application No.

09/689,366

Applicant(s)

ROTHE ET AL.

Examiner

Gerald G Leffers Jr., PhD

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 24 September 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) ☐ they raise the issue of new matter (see Note below);
 - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: 19 and 22.

Claim(s) objected to: _____.

Claim(s) rejected: 17 and 18.

Claim(s) withdrawn from consideration: 20 and 21.

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

GERRY LEFFERS

PRIMARY EXAMINER

Gerald G Leffers Jr., PhD
Primary Examiner
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Advisory Action Attachment

Receipt is acknowledged of an After-Final amendment, filed 9/24/03. The amendment has been entered. Claims 17-18 remain rejected for reasons of record, some of which are repeated below. Claims 19 and 22 are allowed. Claims 20-21 remain withdrawn from consideration as being directed to nonelected inventions.

Continuation of 3. Applicant's reply has overcome the following rejection(s): (i) rejection of claim 22 under 35 U.S.C. 112 for lack of written description as pertains to a binding partner for the c-IAP protein comprising SEQ ID NO: 2, (ii) claim 28 has been cancelled, obviating an outstanding rejection under 35 U.S.C. 112 1st paragraph for New Matter.

Continuation of 5. does NOT place the application in condition for allowance because: applicants response merely argues many of the same points addressed earlier in the same way. Consequently, the examiner's response to those arguments from the previous office action are incorporated here by reference. The response essentially argues: **1)** the written description requirement does not require the applicant to describe exactly the subject matter claimed, only that the description allows a person of ordinary skill in the art to recognize applicants invented that which is claimed, **2)** the rejected claims expressly recite that the claimed protein comprise a specific domain that binds TRAF1 or TRAF2, **3)** the specification expressly informs that the invention includes deletion mutants of cIAP-1 (SEQ ID NO: 2) that have a disclosed cIAP activity, **4)** the specification discloses that the cIAP BIR domains represent novel protein::protein interaction domains, and which can be mixed and matched to form functional chimeras, **5)** the

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specification teaches in experimental detail how to screen for interactions of such BIR domain-containing proteins with proteins like TRAF1 and TRAF2, 6) the specification conveys both possession and use of proteins comprising the specifically recited cIAP BIR domains, 7) the examiner's discussion of protein structure and function is not on point and inapt, 8) the action resorts to drama and obfuscation re: referring to the Holy Grail/King Arthur and determining the 3 dimensional structure of anything, 9) those skilled in the art would have to close their eyes to not recognize applicants' disclosure of cIAP BIR domains (e.g. SEQ ID NO: 9) as protein::protein interaction domains that bind TRAF1 and TRAF2, 10) the skilled artisan would readily recognize the specification teaches how to screen for TRAF binding, 11) Takahashi et al (J. Biol. Chem. April 3, 1998, Vol. 273, pages 7787-90) teach that a single cIAP BIR domain is sufficient to bind and inhibit caspase-7.

As indicated above, most of applicants' arguments have been dealt with previously. Arguments directed to methods of screening for proteins (e.g. hybrid proteins encompassed by claim 18) that bind a TRAF1 or TRAF2 protein are better suited to an enablement rejection. The instant rejection is for a lack of written description of a sufficient number the proteins embraced by claims 17-18 that meet the functional limitations of the claims so as to indicate to the skilled artisan that applicants were in possession of the broadly claimed genus of such proteins. The fact remains that applicants have not provided any data to suggest that any single BIR domain from SEQ ID NO: 2 binds specifically to TRAF1 or TRAF2. While it is true that Takahashi et al and others have shown that a single BIR domain from a different protein (i.e. XIAP) will interact with a specific caspase, it is not possible for one to reliably extrapolate the findings for the interaction of the XIAP peptide and caspase-7 to the claimed cIAP-1 proteins and

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TRAF1/TRAF2. Moreover, the Takahashi et al reference is post-filing art and not indicative of the state of the art at the time of the invention, such that its findings, even if applicable, would not have been available to the skilled artisan at the time of filing of the instant application. Nor can one reliably extrapolate from applicants' own data (i.e. that a truncated version of cIAP-1 comprising all three of the BIR domains will bind to TRAF1 and TRAF2) that a protein comprising only one or two of the BIR domains, or a particular hybrid combination of domains from cIAP-1/cIAP-2, will necessarily retain the ability to interact specifically with TRAF1 and/or TRAF2. For example, there is no evidence anywhere of record that the 3rd BIR domain of cIAP-1 (i.e. SEQ ID NO: 9) necessarily interacts with either of the TRAF proteins, as is specifically recited in claim 17. The teachings of the Berendsen reference are on point in that they are provided as an indication of the state of the art at the time of filing with regard to being able to reliably predict based upon primary amino acid sequence alone the structural, and hence, functional characteristics of a protein. Berendsen makes clear that one could not have reliably extrapolated from the primary sequences provided by applicants for cIAP-1 and cIAP-2, as well as the limited experimental data for what proteins did interact with TRAF1/TRAF2, the domains within SEQ ID NOS: 1 & 2 responsible for TRAF interaction. Therefore, the skilled artisan would not have been able to envision those embodiments of the rejected claims that would satisfy the functional limitations of the claims.

Conclusion

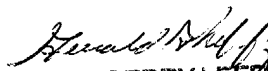
Claims 19 and 22 are allowed. Claims 17-18 remain rejected. Claims 20-21 are withdrawn from consideration as being directed to nonelected inventions.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

 Gerald G Leffers Jr., PhD
Primary Examiner
GERRY LEFFERS
PRIMARY EXAMINER Unit 1636

Ggl